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FEAR OF CANCER RECURRENCE: AN OVERVIEW AND AUSTRALIAN PERSPECTIVE

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Abstract

Fear of cancer recurrence is broadly defined as the fear or worry that cancer could return or progress in the same place or another part of the body. It is frequently reported as an unmet need by cancer survivors, and does not appear to diminish with time since diagnosis and treatment completion. Fear of cancer recurrence is almost universal among cancer survivors, and those experiencing high levels of fear of cancer recurrence experience difficulties moving on with life after diagnosis and treatment, and have poorer quality of life. It is a prevalent and persistent issue for cancer survivors, with significant costs for the individual, family and society. Those who are younger have greater symptom burden and greater psychological distress are likely to have higher fear of cancer recurrence. Few intervention studies have been reported in the literature to date to guide health service provision. However, several studies are currently underway in Australia to develop empirically tested theory-driven interventions.

Improved medical treatments for cancer have led to higher survival rates; the five-year relative survival in Australia is currently 66% for all cancers combined.¹ In response, research has increasingly focused on longerterm survivorship issues. One of the most prevalent and severe unmet supportive care needs in cancer survivors, that does not appear to diminish with time since diagnosis, is for help with fear of cancer recurrence.^{2,3} This review aims to present current research on this, together with interventions currently under investigation from an Australian perspective.

Conceptualisation and measurement of fear of cancer recurrence

Conceptualisation of fear of cancer recurrence is still evolving, with no widely-accepted understanding of its nature or clinical significance. However, Vickberg's definition of fear of cancer recurrence: "The fear or worry that cancer could return or progress in the same place or another part of the body," has frequently been employed.³ Fear of cancer recurrence has been characterised as multidimensional, comprising emotional, cognitive and behavioural reactions.⁴ Numerous measures have been published that attempt to evaluate the nature and severity of fear of cancer recurrence, but each uses a slightly different approach, employing different definitions and emphasising different aspects of fear of recurrence. Consequently, the setting and purpose of evaluating fear or recurrence should be considered when selecting a measure.⁵

The clinical significance of fear of cancer recurrence is unclear. Despite an apparent association between fear of recurrence and quality of life (QOL), little work has investigated the level or severity of fear of recurrence at which it begins to impact daily life. To date, one study has attempted to establish a clinical cut-off score for fear of cancer recurrence (on the Fear of Cancer Recurrence Inventory Severity Subscale).6,7 However, the purposedesigned diagnostic interview used in that study has not vet been validated, so the proposed cut-off of 13 can only be considered preliminary. There is some evidence suggesting this cut-off has strong sensitivity but poor discrimination, and may falsely identify many people with clinical levels of fear of cancer recurrence.⁸ In the absence of established clinical cut-offs, researchers have employed more descriptive approaches. For example, Lebel et al considered women with breast or ovarian cancer had moderate to high levels of fear of recurrence when they endorsed more than 50% of the 22 items on the Fear of cancer recurrence questionnaire with a 4 or 5 (item range 1-5), and scored in the clinical range which involves total score ≥26, range 0-75 on the validated Impact of Event Scale.9,10,11

Prevalence of fear of cancer recurrence

Some degree of fear of cancer recurrence is reported by almost all cancer survivors and their caregivers.^{12,13} For example, of 1442 Australian adult cancer survivors diagnosed with one of the eight most common cancers, 46% worried about their cancer returning or getting worse

at 12 months post-diagnosis.¹⁴ A recent systematic review found that across different cancer sites and assessment strategies: 39-97% of cancer survivors reported some degree of fear of recurrence (on average 73%); 22-87% reported moderate to high fear of recurrence (on average 49%); and 0-15% reported high fear of recurrence (on average 7%).¹⁵ Some studies have reported even higher levels of fear of recurrence among caregivers than patients.¹² The wide range in prevalence estimates appears due to several factors, including different definitions such as fear of progression versus fear of recurrence, together with measures and sample characteristics.¹⁶

Fear of cancer recurrence does not always decrease with time, even when the risk of recurrence is low.15,16 The above-mentioned systematic review identified 21 crosssectional studies exploring associations between time since diagnosis and fear of cancer recurrence severity, with only one study reporting a significant association,^{15,17} reinforcing the stability of fear of recurrence over time.¹⁸ In their longitudinal study, Ghazali et al reported that among head and neck cancer survivors: approximately 50% did not experience significant levels of fear of recurrence; approximately 20% experienced significant levels of fear of recurrence intermittently; and approximately 30% experienced stable and significant levels of fear or recurrence over time.¹⁹ Furthermore, for this last group, fear of recurrence scores did not fluctuate, remaining high over time.

Predictors of fear of cancer recurrence

Younger age is consistently associated with higher fear of cancer recurrence.^{3,13,20} There is inconsistent evidence that females, minority groups, and those with lower education, lower income, or in employment, experience higher fear of recurrence.¹⁵ Fulfilling a caregiving role, such as being a young mother, has been associated with higher fear of recurrence,^{21,22} although another study found no association between having children, attitudes to future pregnancy, and fear of recurrence in young breast cancer survivors.²³ Thus the contribution of many socio-demographic variables to fear of cancer recurrence remains uncertain.

Counter-intuitively, fear of cancer recurrence is not clearly linked to prognostic indicators such as stage of disease and treatment received.^{16,24} For example, in one review, prognostic indicators including TNM stage, prostatespecific antigen level, Gleason score and presence of positive margin, were positively associated with fear of cancer recurrence in 11 studies, but 16 studies reported no association.¹⁵ Similarly, having had a recurrence or metastatic diagnosis was significantly associated with fear of recurrence in five studies, but unrelated in four. However, high subjective risk, illness perceptions and intrusive thoughts have consistently been associated with higher fear of recurrence, while optimism has been associated with lower fear of recurrence.^{15,16,25} This suggests that assessment and review of unrealistically high subjective risk, may be a strategy for combating fear of cancer recurrence.²⁶

There is strong evidence for a relationship between fear of cancer recurrence and symptom experience, particularly global symptom burden, pain, fatigue and body image concerns.^{15,16,24} These symptoms may remind survivors of their cancer diagnosis,²⁷ and be interpreted as possible signs of recurrence, thereby increasing fear of cancer recurrence. These results suggest that education about the meaning of symptoms and those likely to be related to recurrence may be helpful.

With regards to psychological predictors of fear of cancer recurrence, general distress, depression, anxiety and avoidance have been associated with higher fear of recurrence.^{15,16,25} Some studies have also reported an association between fear of cancer recurrence and diagnosed anxiety or psychiatric conditions such as post-traumatic stress disorder, global anxiety disorder, hypochondriasis and obsessive compulsive disorder,^{23,28,29} although most cancer survivors do not appear to suffer such co-morbidities.²³ The relationship between psychological factors and fear of cancer recurrence is most likely bi-directional.¹⁵

Consequences of fear of cancer recurrence

Adjustment to the possibility of cancer recurrence is sometimes reported as more problematic than adjustment to the initial diagnosis.³⁰ High fear of recurrence levels have been shown to have a negative impact on QOL, psychological adjustment, emotional distress and anxiety, ability to establish future goals and plans, and carer QOL.^{15,16,25,31} However, Simard et al argue that the large number of concepts explored means the evidence base for any one psychological impact is weak.¹⁵ Furthermore, Lebel et al showed that change in fear of cancer recurrence did not lead to changes in distress and intrusions/avoidance over time.³²

Fear of cancer recurrence has been associated with higher use of medical services, including complementary and alternative medicines, and increased medical costs.^{13,33} For example, in Australian early-stage breast cancer survivors approximately four years post-diagnosis, those with higher fear of cancer recurrence were more likely to have unscheduled GP visits and use complementary therapies.¹³ These women were also more likely to engage in breast self-examination, but avoid formal screening measures such as mammograms and ultrasounds, potentially compromising health outcomes.¹³ Thus the impact of high fear of recurrence is wide-ranging, with potential costs to the individual, the family and wider society.

Unmet need for help with managing fear of cancer recurrence

Despite the high prevalence and potential cost of fear of cancer recurrence, survivors report high levels of unmet need for help managing this fear, suggesting many cancer services are not currently providing adequate care in this area. A multi-centre Australian study (n=388) found that fear of cancer recurrence was survivors' greatest area of unmet need, with 26% reporting moderate to high unmet need for help with this fear.34 The need for effective interventions for fear of recurrence has been recognised by oncology health professionals. In a survey of 141 Australian medical and radiation oncologists, surgeons, nurses, palliative care specialists, psychiatrists, psychologists and social workers, 33% reported spending more than 25% of follow-up consultation time discussing fear of cancer recurrence, 46% found dealing with this challenging and almost all were interested in further training for managing patients with this fear.35 These results emphasise the need for developing effective, theory and evidencebased treatments for fear of cancer recurrence.

Theoretical perspectives on fear of cancer recurrence

Several theoretical models have been previously used to explain fear of cancer recurrence, though none is universally accepted. These are presented below.

Theory of uncertainty in illness

Although uncertainty is not the same as fear of cancer recurrence, aspects of Mishel's theory of uncertainty in illness may be relevant to understanding this fear.36,37 According to this theory, uncertainty is the inability to determine the meaning of illness-related events.³⁶ It is generated when there is inconsistency, randomness, complexity, unpredictability and little information about the illness, its treatment, and related events including symptoms.36 Integrating uncertainty into one's life and directing it in a desired direction such as reduced uncertainty is an essential task in adaption.³⁷ Uncertainty about the possibility of cancer recurrence is similarly triggered by intrusive, unpredictable and random events.³⁸ The difficulty with this causal explanation of fear of cancer recurrence is that some degree of uncertainty about recurrence likely exists for all cancer survivors, yet not all cancer survivors develop clinically significant levels of fear of recurrence.

Self-regulation of illness/common sense model

The self-regulation of illness or common sense model proposes that when individuals are confronted with a health threat, an illness representation is activated consisting of cognitive factors, meaning perceived personal risk of recurrence and emotional considerations including worry about the cancer returning, anxiety about cancer itself, and regret about treatment decisions and these motivational processing systems, act together to guide coping behaviours.4,39,40 Lee-Jones et al hypothesised that survivors who viewed their cancer as chronic, with negative and uncontrollable consequences, were likely to engage in more emotional processing of health threats and have higher fear of cancer recurrence.⁴ There is some evidence for the common sense model in dealing with fear of recurrence; individuals who believe they are vulnerable to cancer are more emotionally aroused by somatic stimuli and display higher levels of fear of recurrence, while adaptive coping strategies are associated with lower fear of recurrence.4,41-43 However, this model does not address how survivors come to have negative cognitive and emotional responses to cancer.

Self-regulatory executive function model of anxiety disorders

The self-regulatory executive function model addresses maintaining factors associated with anxiety disorders and has been used to effectively treat health anxiety. 44,45-47 The model proposes the cognitive attentional syndrome which consists of: self-focused attention, worry and rumination; attentional bias towards threat-related information; and maladaptive coping behaviours including suppression, avoidance and minimisation. Cognitive attentional syndrome impairs flexible selfcontrol and prevents corrective learning experiences, leading to increased and persistent distressing emotions. The self-regulatory executive function model argues that beliefs about one's thoughts underlie activation of cognitive attentional syndrome.⁴⁴ That is, those who believe worry is important and may impact the outcome (e.g. "If I worry I will be prepared") are more likely to engage in cognitive attentional syndrome, in turn intensifying fears and worries about cancer returning. Research has shown that anxious cancer patients display an attentional bias towards threatening stimuli,48-50 and fear of recurrence level appears to be associated with metacognitions and beliefs about cancer vulnerability.^{4,41-43} The self-regulatory executive function model appears particularly applicable to fear of recurrence because the belief that cancer might recur is not entirely irrational, and hence a focus on cognitive processes rather than content could be advantageous, and it explains why elevated emotional responses after cancer diagnosis are maintained.40

Relational frame theory and acceptance and commitment therapy

Acceptance and commitment therapy,⁵¹ based on relational frame theory, focuses on increasing cognitive flexibility and emphasises accepting feelings, thoughts

and sensations when attempts to control them are counterproductive and prevent the individual acting in line with desired goals and values.^{51,52} Acceptance and commitment therapy can address the existential issues that arise when cancer is diagnosed, as it aims to help clients develop more clarity about what is important to them and to establish behavioural goals in accordance with those values.⁵¹ Acceptance and commitment therapy has recently been applied in the cancer context with promising results.⁵³⁻⁵⁵ Also, while it is yet to be empirically evaluated in randomised control trials, Australian psychosocialoncology health professionals report acceptance and commitment therapy offers clinically useful strategies for treating fear of cancer recurrence.³⁵

Intervention studies

The AFTER intervention (Adjustment to Fear, Threat or Expectation of Recurrence) was one of the first psychological interventions specifically designed to address fear of cancer recurrence in head and neck cancer patients.56,57 This intervention, based on the common sense model, consisted of six face-to-face individual sessions with a specialist nurse and encouraged participants to discuss the likelihood of recurrence, express cancer recurrence-related fears, their triggers and consequences. The manualised sessions also covered excessive checking behaviours and illness beliefs and representations.56,57 Two assessments were carried out before the intervention, at three and seven months post-treatment completion, and two after, at 11 and 15 months post-treatment completion. The intervention group maintained general anxiety levels before and after the intervention, while the control group had increased anxiety. There was a statistically significant improvement in fear of cancer recurrence for the intervention versus control participants immediately post-intervention, that was not maintained at 15 months. A significant limitation of the trial was its lack of statistical power. Also, participants were not screened for high levels of fear of cancer recurrence prior to study entry, and together with using a three-item fear of cancer recurrence measure, this may have contributed to the mild effects found.

Lebel et al developed a manualised six week cognitive existential group intervention targeting fear of cancer recurrence based on the common sense model,⁹ Mishel's uncertainty in illness theory, cognitive models of worry and components of a cognitive-existential group intervention.⁵⁸ Stage I-III breast and ovarian cancer patients were eligible for this single-arm pilot if they reported clinically significant fear of cancer recurrence levels (discussed above) and had completed primary treatment. Immediately postintervention, women experienced significantly lower fear of cancer recurrence, plus significantly lower cancer-specific distress, uncertainty and negative QOL. Changes were maintained at three-month follow-up. These preliminary positive results are tempered by 12 of 56 participants (21%) dropping out over the course of the intervention.

Several studies investigated interventions targeting concepts similar to fear of cancer recurrence. Herschbach et al compared cognitive behaviour group therapy or supportive-experiential group therapy with usual care over 12 months on fear of progression,59,60 with both intervention groups showing significant reductions in fear of progression over time compared to controls. Heinrichs et al similarly showed that a couple-skills intervention reduced fear of progression compared to a control cancer education program in breast and gynaecological cancer patients and their carers.⁶¹ However, these benefits were not maintained at follow-up, 16 months post-diagnosis. A third study reported that a nurse-led telephone intervention for uncertainty management in long-term breast cancer survivors increased cognitive reframing and cancer knowledge compared to usual care controls.38

Though they did not specifically target fear of cancer recurrence, in a single arm pilot study Chambers et al found a non-significant trend for decreased fear of recurrence in Australian men diagnosed with advanced prostate cancer, who participated in an eight-week mindfulness-based program three months post-treatment completion.⁶² Lengacher et al reported on a six-eight session Mindfulness-Based Stress Reduction group program designed to improve psychological status generally.⁶³⁻⁶⁵ Significant improvements were seen in fear of recurrence, as well as depression and anxiety, though no long-term data has been published.⁶³ Thus further research evaluating fear of cancer recurrence specific interventions is required.

There are two interventions currently underway in Australia which specifically target fear of cancer recurrence.* The first is a multi-centre randomised trial comparing a novel psychological intervention called 'Conquer Fear' to relaxation training for cancer patients.⁴⁰ Both interventions are manualised and delivered in five sessions over 5-10 weeks by trained psychologists and psychiatrists. Eligible participants are breast, colorectal or melanoma cancer survivors who have completed hospital-based treatment between two months and five years prior, and report a score in the clinical range on the Fear of Cancer Recurrence Inventory Severity Subscale. Conquer Fear incorporates aspects of the self-regulatory executive function model and relational frame theory, together with the common

^{*}A review of the Australian and New Zealand Clinical Trials Registry on 24th July 2014, found only two studies registered with fear of cancer recurrence as the primary outcome measure. The authors acknowledge other Australian groups may be undertaking research on novel interventions or therapeutic approaches for managing fear of cancer recurrence, but at the time of writing this article they were not registered with Australian and New Zealand Clinical Trials Registry

sense model, to provide a novel metacognitive account of fear of recurrence. The sessions cover attention training, detached mindfulness, meta-cognitive therapy, values clarification and psycho-education to help cancer survivors change how they regulate and respond to thoughts about cancer recurrence. The relaxation training arm focuses on both internal and external stressors associated with fear of recurrence, and teaches progressive and passive muscle relaxation, meditative relaxation, visualisation and 'quick relaxation' techniques. The primary outcome measure is fear of cancer recurrence as measured by the Fear of Cancer Recurrence Inventory, and participants are followed up for six months after intervention completion. This trial is currently recruiting and due for completion in 2016. The second trial in progress is a randomised trial comparing a novel psycho-educational intervention for high-risk melanoma cancer patients to usual care.66 The psycho-educational intervention comprises a tailored, psycho-educational booklet and three individual, telephone-based counselling sessions delivered by a clinical psychologist focused around their high-risk melanoma clinic appointments. The primary outcome is fear of cancer recurrence as measured by the fear, assessed two-three weeks after their first high risk clinic appointment and again at five and 11 months afterwards.

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